9. **(Twice Amended)** The method of Claim 8, wherein said effective amount of a compound that inhibits the production or release of intercellular reactive oxygen metabolites (ROM) is between about 0.05 mg and about 50 mg per dose.

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10. **(Twice Amended)** The method of Claim 8, wherein said effective amount of a compound that inhibits the production or release of intercellular reactive oxygen metabolites (ROM) is between about 1 microgram/kg and about 100 microgram/kg of patient weight per dose.

REMARKS

Claims 1, 8-13 are pending. Claims 1, 9 and 10 have been amended. Claim 13 is cancelled without prejudice. No new matter has been added herewith. Entry of these amendments and reconsideration of the above-referenced application is respectfully requested.

The changes made to Claims 1, 9 and 10 by the current amendment, including insertions and ~~deletions~~, are shown on an attached sheet entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this amendment.

Telephonic Interview

Applicants thank the Examiner for the courtesy shown during the telephonic interview conducted on November 20, 2002. Although no agreement was reached regarding the pending claims, the Examiner did agree to provide Applicants with an Advisory Action after reviewing the present response.

The Amendment filed April 25, 2002 Does Not Add New Matter

Applicants inadvertently misspelled "diphenylene iodonium" in the specification as originally filed. Applicants amended the specification in the previous Amendment to disclose the correct chemical name of the compound DPI as "diphenylene iodonium" in the Amendment filed April 25, 2002. The Examiner has objected to this amendment under 35 U.S.C. § 132, because it allegedly introduced new matter. The Examiner also alleges that Applicants failed to assert that no new matter was introduced by way of the Amendments of April 25, 2002. Applicants disagree.

Applicants consistently used the abbreviation "DPI" for diphenylene iodonium such that one of ordinary skill in the art would know that the compound disclosed in the present application was diphenylene iodonium. This usage is sufficient to provide notice to one of ordinary skill in the art that Applicants intended to disclose "diphenylene iodonium" in the

specification as the full name of the compound abbreviated as "DPI". For example, at page 26, lines 17-20, Applicants refer to DPI as used by Miesel, et al., Free Radical Biology & Medicine, Vol. 20, 75-81, 1995 (Ref. No. 41, PTO 1449 submitted Nov. 27, 2000)[1]. A copy of the reference is provided for the Examiner's reference. As shown in the reference, diphenylene iodonium is the source for the abbreviation "DPI." See Miesel, et al., pg. 75, abstract. Because Applicants used the art-recognized abbreviation of DPI in the specification, Applicants submit that they are now entitled to correct the minor typographical error now without introducing new matter into the present application. As such, Applicants request that the Examiner withdraw the objection.

Further, Applicants note that there is no such compound as "diphenylionodonium." Applicants submit a page from the Sigma™ catalog (page 418) supporting this statement. One of ordinary skill in the art would immediately recognize that a typographical error had been made in the specification as filed and further would understand that Applicants use of the abbreviation "DPI" referred to diphenylene iodonium.

Additionally, Applicants clearly asserted that no new matter was added by way of the amendments in the submission of April 25, 2002. Applicants direct the Examiner to page 2 of that paper for support of this assertion.

Claims 1 and 8-13 are fully enabled

The Examiner has rejected Claims 1 and 8-13 under 35 U.S.C. § 112 as allegedly not being enabled by the specification. Specifically, the Examiner argues that the specification does not teach the use of DPI to activate cytotoxic lymphocytes. The specification does, however, clearly demonstrate that DPI administration with a cytokine is effective to protect cytotoxic lymphocyte from oxidative inhibition in the presence of monocytes. Although Applicants disagree with the Examiner's position, to facilitate allowance of the claims, independent Claim 1 has been amended to remove the term "activate." As such, this amendment obviates that rejection.

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1 Applicants note that Miesel, et al. used diphenylene iodonium chloride. Applicants submit that the compound disclosed in Miesel, et al. is merely the salt form of DPI and that no significant difference exists between the compound disclosed in the present application and that in the reference.

Claims 1 and 8-13 are fully supported by the specification

The Examiner has rejected Claims 1 and 8-13 under 35 U.S.C. § 112 as allegedly not being described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventor was in possession of the claimed subject matter at the time the application was filed. Specifically, the Examiner has taken issue with the limitation "cytotoxic lymphocyte." Applicants disagree with the Examiner on this issue regarding the term "cytotoxic lymphocyte." Nevertheless, to advance the present case to allowance, Applicants have amended independent Claim 1 to recite NK cells and cytotoxic T lymphocytes rather than cytotoxic lymphocytes. Protection of NK cells and cytotoxic T lymphocytes is discussed throughout the specification, for example, at page 23, lines 22-28.

In light of these amendments, Applicants submit that the pending claims are fully supported by the specification. Thus, Applicants request that this rejection be withdrawn.

The Examiner has also rejected Claims 9 and 10 for reciting "a compound that inhibits the production and release of intercellular reactive oxygen metabolites." These claims have been amended to recite "a compound that inhibits the production or release of intercellular reactive oxygen metabolites." The recitation of a compound that inhibits the production or release of intercellular reactive oxygen metabolites is supported by the claims as originally filed. Applicants submit that these amendments obviate the grounds for rejection of Claims 9 and 10.

CONCLUSION

For all of the above reasons, Applicants respectfully request withdrawal of all rejections and allowance of the pending application.

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is invited to initiate the same with the undersigned.

A one-month extension of time is requested. Please charge any additional fees or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 25 NOV 2002

By: _____

James J. Mullen III, Ph.D.
Registration No. 44,957
Attorney of Record
620 Newport Center Drive
Sixteenth Floor
Newport Beach, CA 92660
(619)235-8550

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Please cancel Claim 13, without prejudice.

Please amend Claims 1, 9 and 10 to read as follows:

1. **(Twice Amended)** A method for ~~activating and~~ protecting NK cells and cytotoxic T lymphocytes from oxidative inhibition in the presence of monocytes (MO), comprising:

identifying a patient in need of enhanced NK cell and cytotoxic T lymphocyte activity; and

administering to the patient a composition comprising an amount of diphenylene iodonium (DPI), effective to ~~activate and~~ protect NK cell and cytotoxic lymphocyte function in the presence of MO.

9. **(Twice Amended)** The method of Claim 8, wherein said effective amount of a compound that inhibits the production ~~and~~ or release of intercellular reactive oxygen metabolites (ROM) is between about 0.05 mg and about 50 mg per dose.

10. **(Twice Amended)** The method of Claim 8, wherein said effective amount of a compound that inhibits the production ~~and~~ or release of intercellular reactive oxygen metabolites (ROM) is between about 1 microgram/kg and about 100 microgram/kg of patient weight per dose.

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